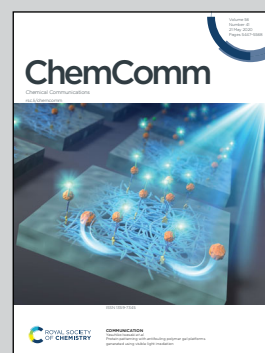[Eu]

Showcasing research from Rosario Herranz's group at the Instituto de Química Médica (CSIC) in Madrid, Spain and Photochemistry and Photobiology group (FQM-247) of the University of Granada, Spain

Smart lanthanide antennas for sensing water

Two new types of simple and selective antennas of the luminescence of the lanthanide cations Eu³⁺ and Tb³⁺ have been discovered that behave as highly sensitive water sensors.

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Smart lanthanide antennas for sensing water†

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Two new families of lanthanide antennas are described. 8-Methoxy-4,5-dihydrocyclopenta[de]quinolin-2(1H)-one phosphonates or carboxylates behave as selective antennas exhibiting Eu^{3+} luminescence in organic solvents, while quinolin-2(1H)-one analogues selectively sensitize the Tb^{3+} emission. These emissions are quenched by H_2O addition. Based on this behaviour, the new lanthanide antennas can be used as highly sensitive water sensors.

Water is the most common impurity in organic solvents and its detection is important in diverse industrial processes, such as pharmaceutical and petrochemical manufacturing and food processing, and in the fine chemical industry.[1–4] Classic and current industrial methods for the determination of H_2O content are based on electrochemical and electrophysical sensing mechanisms, but optical sensors are emerging as sensitive, faster, and robust humidity sensors, in particular luminescent ones.[5] The emission characteristics of lanthanide cations (Ln^{3+}) are particularly interesting for sensor development, because they emit narrow and element specific bands, not perturbed by the environment, due to f–f electronic transitions, which are generally Laporte forbidden.[6] This forbidden character is responsible for the low lanthanide absorbance and their long luminescence lifetimes that result in interesting and useful applications in time-resolved luminescence techniques. The low absorbance of Ln^{3+} can be overcome by indirect excitation

through organic chromophores, which transfer energy to these cations by an "antenna effect".[7,8] Interestingly, the luminescence of lanthanide cations is very sensitive to quenching by water molecules.[9,10] This effect can be exploited to develop water sensors, paving the way for a new application of lanthanide probes, since reports on the use of this strategy to design water sensors have been very scarce.[2,11–14]

Even though β-dicarbonyl compounds are among some of the most studied ligands for lanthanides and quinolin-2-ones are among the most widely used sensitizing antennas,[15–20] up to date, no quinolin-2(1H)-one-derived antennas capable of assembling directly with lanthanide ions in solution have been described. In general, antennas that directly assemble lanthanide cations are bulky multidentate ligands able to coordinate the cations with a high coordination number.[7,8,17,21,22] However, herein we explore the potential of small-size quinolin-2(1H)-one derivatives with β-dicarbonyl character, concretely, 8-methoxy-4,5-dihydrocyclopenta[de]quinolin-2(1H)-ones **1** and **2**[23] and their carbostyril analogues **3** and **4** (Chart 1) as self-assembled lanthanide sensitizers. Importantly, such complexes exhibit an

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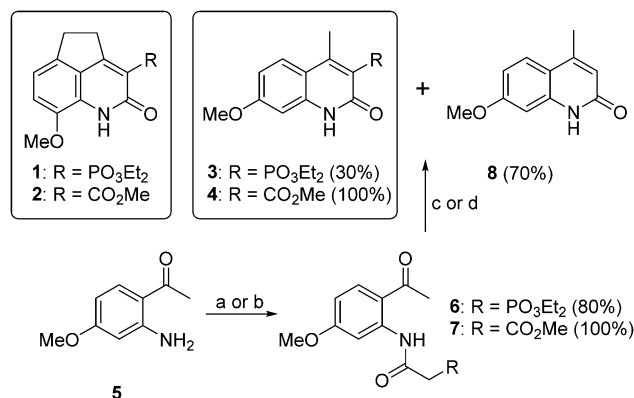[c] *Instituto de Química Física Rocasolano, IQFR-CSIC, Serrano 119, Madrid 28006, Spain*

Chart 1 8-Methoxy-4,5-dihydrocyclopenta[de]quinolin-2(1H)-ones **1** and **2** and synthesis of the carbostyril analogues **3** and **4**. (a) (EtO)$_2$OPCH$_2$CO$_2$H, HATU, DIPEA, CH$_2$Cl$_2$; (b) MeCO$_2$CH$_2$COCl, CH$_2$Cl$_2$; (c) NaH, DMF; and (d) K$_2$CO$_3$, MeOH, 70 °C MW.

extraordinary ability to sense H_2O impurities in organic solvents. Analogues **3** and **4** were specifically designed taking into account the fact that substituent positions affect their absorption spectra, and hence the lanthanide sensitizing efficiency. Specifically, previous studies on lanthanide antennas derived from quinolin-2(1H)-ones (carbostyrils) have shown that the MeO substituent at position 7 gave the highest molar absorption coefficient (ε).[18,24] These quinolin-2(1H)-ones were synthesized from the commercial 2-amino-4-methoxy-acetophenone (**5**), by acylation with diethyl phosphonoacetic acid for **3** or methyl 3-chloro-3-oxopropionate for **4**, followed by base promoted cyclization in the presence of NaH or K_2CO_3 (Chart 1). It is interesting to note that in the cyclization of the intermediate carboxamide **6** in the presence of NaH the phosphonate **3** was obtained as a minor compound (30%), along with **8** (70%), which resulted from the removal of diethyl hydrogen phosphite. However, the carboxylate analogue **4** was obtained quantitatively.

The UV absorption and emission parameters of compounds **1**–**4** were determined in solvents of increasing polarity from toluene to H_2O and are summarized in Table S1 (ESI†). The four compounds showed two absorption maxima with just slight changes in energy and molar absorptivity values. The dihydro-cyclopenta[de]quinolin-2(1H)-one derivatives **1** and **2** emitted at longer wavelengths (30–100 nm) than **3** and **4** and their emission maxima were bathochromically shifted with increasing solvent polarity (≈ 40 nm from toluene to H_2O). Interestingly, the fluorescence quantum yields (Φ_F) of the four compounds significantly increased with solvent polarity.

Then, we tested the ability of compounds **1**–**4** to directly bind lanthanide ions in solution, sensitizing their emission. First we carried out a qualitative evaluation by observing the emission of **1**–**4** (0.1 mM) in CH_3CN upon addition of $TbCl_3$, $EuCl_3$, $DyCl_3$ or $SmCl_3$ (0.1 mM) on a UV transilluminator ($\lambda_{ex} = 365$ nm, Fig. 1), and then we carried out a quantitative analysis in a spectrofluorometer. Regarding compounds **1** and **2**, we collected emission spectra of these dyes (54 µM) dissolved in CH_3CN after the addition of 1 and 2 equivalents of $TbCl_3$, $EuCl_3$, $DyCl_3$ and $SmCl_3$ (ESI,† Fig. S1 and S2). The addition of $EuCl_3$ led to the appearance of significant bands of sensitized luminescence of the lanthanide cation, mainly the $^5D_0 \rightarrow {}^7F_2$ Eu^{3+} band at 612 nm (Fig. 2A and B). We also performed a more systematic titration of solutions of **1** and **2** in CH_3CN with
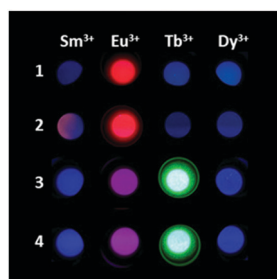

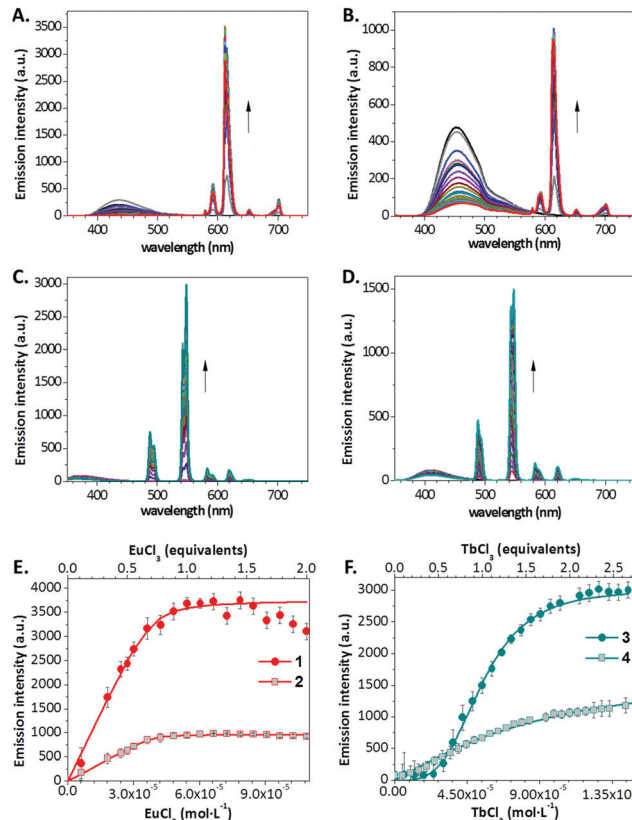Fig. 2 Titration spectra of solutions (54 µM) of the 8-methoxy-4,5-dihydrocyclopenta-[de]quinolin-2(1H)-ones **1** (A) and **2** (B) with increasing equivalents (0–2) of $EuCl_3$ and the carbostyril analogues **3** (C) and **4** (D) with increasing equivalents (0–4) of $TbCl_3$. (E) Eu^{3+} luminescence of its complexes with **1** and **2** at 612 nm as a function of added $EuCl_3$ equivalents and molar concentration (0–2). (F) Tb^{3+} luminescence of its complexes with **3** and **4** at 545 nm as a function of added $TbCl_3$ equivalents (0–2.5). Titrations were carried out in triplicate. Error bars represent standard deviation values.

increasing concentrations of $EuCl_3$, showing, in both cases, that luminescence saturation is achieved for amounts of europium close to 1 equivalent (Fig. 2E). Besides, experimental data fit satisfactorily to a binding model considering the possibility of single or multiple binding events (see the ESI†). The fittings provided values for the apparent binding constants of 1.1×10^6 and 3.1×10^6 for the complexes formed with compounds **1** and **2**, respectively. Interestingly, stoichiometries between 1 and 2 molecules of antenna per lanthanide ion are obtained for both complexes, indicating that a mixture of complexes with different stoichiometries may coexist in solution. In this regard, a double emission band (612 and 615 nm) was detected, whose relative intensity varied with the antenna:$EuCl_3$ ratio, pointing out probably to the diverse contribution of the different complexes (Fig. S3, ESI†). The absolute luminescence quantum yields of the respective Eu^{3+} complexes of **1** and **2**, measured with an integrating sphere, were 0.24 and 0.08, respectively. With the addition of $EuCl_3$, the emission of the antenna decreased, due to energy transfer toward the cation, with the concomitant increase in the Eu^{3+} emission. The luminescence lifetimes (τ) of the Eu^{3+}

Fig. 1 Luminescence of antennas **1**–**4** (0.54 µM) in CH_3CN after addition of $TbCl_3$, $EuCl_3$, $DyCl_3$ or $SmCl_3$ (0.1 mM), upon UV irradiation on a transilluminator ($\lambda_{ex} = 365$ nm).

emission for the complexes with **1** and **2** were 0.55 ± 0.04 and 0.24 ± 0.01 ms, respectively.

In the titration of the carbostyril derivatives **3** and **4** (54 μM) in CH$_3$CN with TbCl$_3$, EuCl$_3$, DyCl$_3$ and SmCl$_3$, significant energy transfer was only observed for the Tb^{3+} cation, which was observed mainly in its $^5D_4 \rightarrow {}^7F_6$ (490 nm) and $^5D_4 \rightarrow {}^7F_5$ (540–550 nm) bands (Fig. 2C and D and Fig. S4 and S5, ESI†). The absolute luminescence quantum yields of the Tb^{3+} complexes of **3** and **4** were 0.21 and 0.08, respectively. The titration study for compounds **3** and **4** with Tb^{3+} showed that luminescence saturation is achieved progressively just after the addition of, at least, 2 equivalents of TbCl$_3$ (Fig. 2F). Titrations with compounds **3** and **4** led to much lower binding constants, down to two orders of magnitude decreased when compared to those of the **1**–**2** antennas with Eu^{3+}, indicating weak stability for these complexes, and poorer fit to the proposed binding model. Besides, the presence of a lag phase upon the increase of luminescence, particularly noticeable for compound **4**, points out to the existence of supramolecular cooperative associations, and indeed, these curves better fitted to a positive cooperativity binding model (see the ESI†). Interestingly, in the case of these Tb^{3+} antennas, no significant influence of the binding equilibrium was observed on the relative intensity of the two bands at 540–550 nm (Fig. S6, ESI†) or on the lifetime of the Tb^{3+} luminescence. The luminescence lifetimes (τ) of the Tb^{3+} emission for the complexes with **3** and **4** were 1.58 ± 0.07 and 1.28 ± 0.06 ms, respectively.

To obtain additional information on the stoichiometry of the coordination of the antennas **1**–**4** with Eu^{3+} and Tb^{3+}, we tried the crystallization of their respective complexes. We obtained good crystals for X-ray analysis of the dihydrocyclopenta[de]quinolin-2(1H)-ones **1** and **2** and their complexes with the Eu(OTf)$_3$ salt.[25] However, we could not obtain good crystals from the complexes of carbostyril derivatives **3** and **4** with Tb^{3+}. The crystal and molecular structures of complexes Eu(**1**)$_2$(H$_2$O)$_4$ and Eu(**2**)$_2$(H$_2$O)$_4$OTf showed a (2:1) antenna:Eu^{3+} stoichiometry (Fig. 3, Fig. S11 and S12, ESI†). In the complex of phosphonate Eu(**1**)$_2$(H$_2$O)$_4$, the cation presented a coordination number of 8, where Eu^{3+} binds two molecules of **1**, through their 2-oxo group and the phosphonate oxygen, and four molecules of H$_2$O. The two molecules of **1** are situated with their molecular planes forming an angle of 50°, on an opposite side to that of

the H$_2$O molecules. In the complex of carboxylate Eu(**2**)$_2$(H$_2$O)$_4$OTf, the Eu^{3+} cation has a coordination number of 9, with the participation of two molecules of ligand **2**, four molecules of H$_2$O and one molecule of triflate. The molecules of **2** are orthogonal with their molecular planes forming an angle of 80° and situated with an opposite orientation. The stoichiometry of these complexes is in good agreement with that obtained in the fittings of the titration curves. Given that the dissociation equilibrium constants lie within the same order of magnitude of the concentration of the antenna and cation used in the titrations, the presence of sub-saturated species (1:1 stoichiometry) is a reasonable result.

In general, the luminescence emission of lanthanide complexes is extremely sensitive to the presence of water or alcohols.[9,10,26] While in aprotic organic solvents, the dihydrocyclopenta-[de]quinolin-2(1H)-ones **1** and **2** are capable of sensitizing Eu^{3+} luminescence and the carbostyril analogues **3** and **4** that of Tb^{3+}, in polar, acidic solvents, such as H$_2$O, MeOH or EtOH, these compounds did not sensitize the lanthanide emission, but maintained their own intrinsic fluorescence emission. This quenching of the luminescence emission is due to the OH vibrations of solvent molecules bound to the central metal. This was confirmed by the large isotope dependency,[26] as evidenced comparing the emission spectra of the Eu^{3+} complex of **1** in MeOH and MeOD (Fig. S8, ESI†). According to Horrocks' equation (see the ESI†), the solvation parameter calculated for the europium complex of **1** (q = 2.8) revealed the presence of three coordinated methanol molecules (Fig. S9, ESI†). This result is in close agreement with the crystallographic results for water molecules, taking into account the larger volume of methanol molecules.

Interestingly, the addition of H$_2$O or MeOH traces (<1%) to 0.1 mM solutions of the Eu^{3+} complexes of **1** or **2** dissolved in CH$_3$CN turned off the characteristic red luminescence of the cation, as exemplarily shown in Fig. 4A. This suggested the potential of these new lanthanide antennas and complexes as H$_2$O sensors. To evaluate this potential, we carried out the titrations of 54 μM solutions of the Eu^{3+} complex of **1** (1:2 stoichiometry) and the Tb^{3+} complex of **3** (1:1 stoichiometry) in CH$_3$CN with increasing amounts of H$_2$O (0–2% v/v). In both cases, the lanthanide luminescence started to decrease with the addition of 0.005% of H$_2$O and completely disappeared with 2% of water. These results fit quite well with the Stern–Volmer equation for quenching (Fig. 4B and C). Simultaneously with the quenching in the lanthanide luminescence emission intensity, the lifetime decreased from 0.49 to 0.14 ms for the Eu^{3+} complex of **1** and from 1.6 to 0.51 ms for the Tb^{3+} complex of **3** (Fig. S10, ESI†). The linear regressions shown in Fig. 4 may be used as calibrations for the determination of water content. The limit of detection values [defined as LOD = (3.3 × SD)/K_{SV},[27] where K_{SV} is the Stern–Volmer constant] were 0.025% for the Eu^{3+} complex of **1** and 0.019% for the Tb^{3+} complex of **3**. These values are comparable to those of the most sensitive water sensors described up to date (in the range of 0.002–0.2% for CH$_3$CN),[2,28] including some lanthanide complexes and metal–organic frameworks (MOFs, in the range of 0.003–0.05%).[12,29,30]
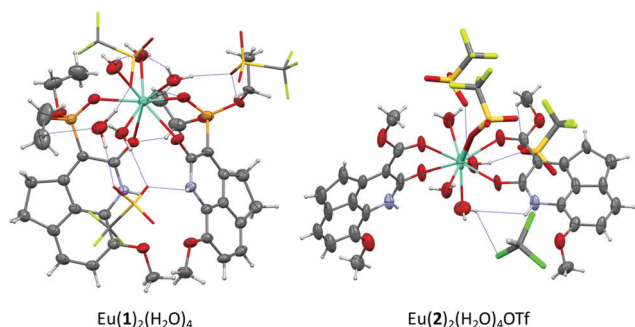

Fig. 3 X-ray structures of the Eu^{3+} complexes with the 8-methoxy-4,5-dihydrocyclopenta[de]quinolin-2(1H)-ones **1** and **2**.

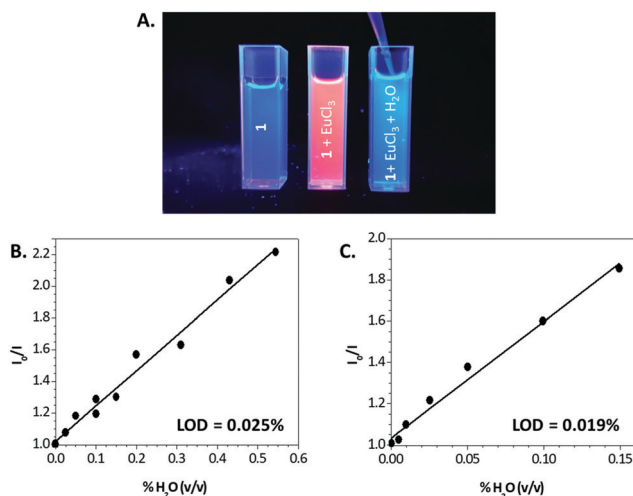Eu(**1**)$_2$(H$_2$O)$_4$ Eu(**2**)$_2$(H$_2$O)$_4$OTf

Fig. 4 (A) Pictures of compound **1** (0.54 μM) dissolved in CH_3CN (left), after addition of 1 equivalent of $EuCl_3$ (center), and after the subsequent addition of traces of H_2O (right), under UV light illumination (λ_{ex} = 365 nm). (B and C) Stern–Volmer plots of the luminescence emission of complexes of **1** with Eu^{3+} (B) and **3** with Tb^{3+} (C) after addition of water.

In conclusion, we have presented herein two new families of lanthanide antennas that, interestingly, are among the smallest lanthanide antennas able to coordinate these cations, sensitizing their luminescence. The first type of antenna is based on 4,5-dihydrocyclopenta[de]quinolin-2(1H)-one phosphonates or carboxylates and selectively sensitizes the Eu^{3+} red luminescence, while the second type, based on carbostyril phosphonate or carboxylate derivatives, sensitizes the Tb^{3+} green emission. Moreover, complexes of these antennas with their respective lanthanides have resulted in highly sensitive sensors for sensing traces of H_2O in organic solvents. Studies on the application of these sensors to determine water content in diverse food industry products are in progress and will be shortly published elsewhere. The ability of our antennas to efficiently sensitize lanthanide luminescence together with their small size will serve as a source of inspiration for the development of a variety of sensors for the study of complex biological systems.

Conflicts of interest

There are no conflicts to declare.

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